SYNTHESIS AND IN-VITRO ANTITUMOR ACTIVITY OF 1-[(INDOL-1-YL)PROP-1-YN-1-YL]PHTHALAZINES AND RELATED COMPOUNDS

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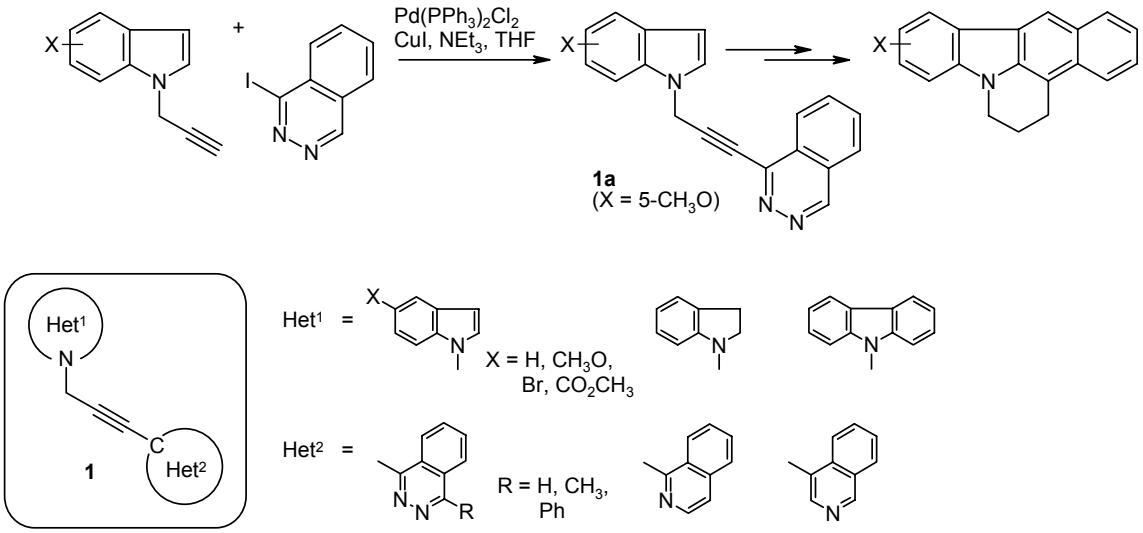
The phthalazine derivative, 1-[3-(5-methoxy-1*H*-indol-1-yl)prop-1-yn-1-yl]phthalazine (**1a**), had been prepared recently as a key intermediate in the synthesis of pentacyclic analogs of the antitumor alkaloid, *ellipticine* [1], via a pathway involving an intramolecular inverse-electron-demand Diels-Alder reaction of indolylalkyl-substituted diazines [2]. In the course of a routine screening, compound **1a** was found to exhibit growth inhibitory activity towards several human tumor cell lines.

Based on the concise synthesis of **1a**, a focused library of compounds featuring the same propyne motif with one electron-rich and one electron-deficient hetarene attached, was now made available. For all new compounds of type **1**, the key step in the reaction sequence is a Sonogashira cross-coupling of an appropriate *N*-propargyl-substituted indole, indoline or carbazole, respectively, with an iodo- or bromohetarene. In the context of this work, also an improved synthesis of 1-iodophthalazine [3] was developed.



[1] For a review on the chemical and biological properties of *ellipticine* and related compounds, see: G. W. Gribble in *The Alkaloids*, Vol. 39, A. Brossi, ed., Academic Press, New York, 1990, p. 239.

[2] N. Haider and J. Käferböck, *Tetrahedron*, **60**, 6495 (2004).

[3] A. Hirsch and G. Orphanos, *Can. J. Chem.*, **44**, 1552 (1966).